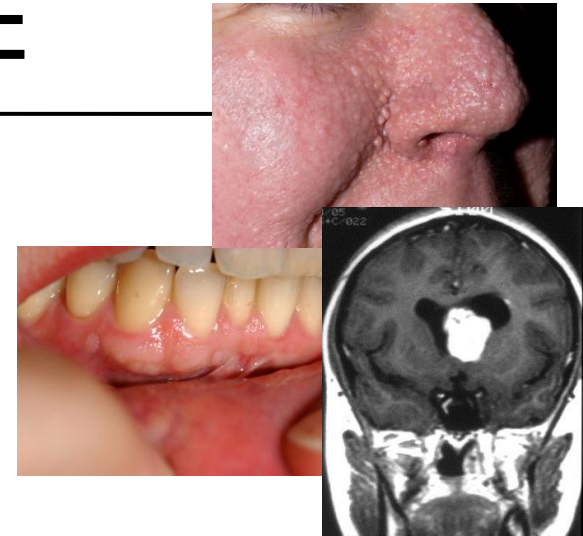


PHYSICAL, PSYCHOLOGICAL AND ETHICAL ISSUES IN CARING FOR INDIVIDUALS WITH GENETIC SKIN DISEASE

Diane C. Seibert, PhD, ARNP, FAANP
Thomas N. Darling, MD, PhD



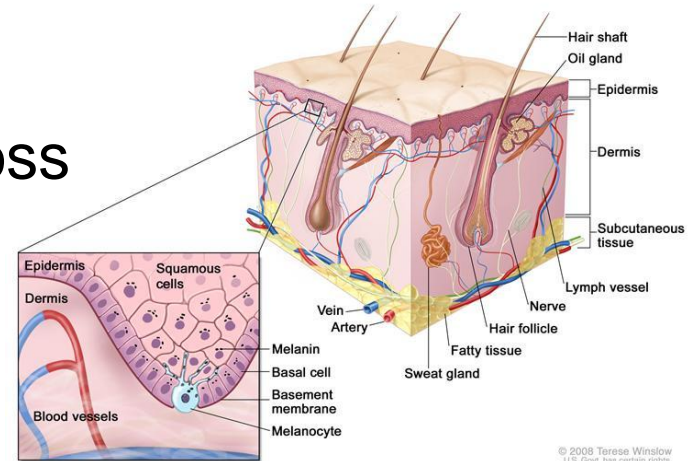
"The views expressed in this poster are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Army, Department of Defense, nor the United States government."

The Skin

1st line of defense between internal & external environments

Healthy skin

- Guards against pathogen invasion
- Protects against excessive water loss
- Regulates body temperature
- Sensation
- Vitamin synthesis



http://www.cancer.gov/cancertopics/pdq/genetics/skin/HealthProfessional#Section_81

Genodermatoses

- Mutations that alter normal skin function
- Usually do not affect lifespan, but often result in social stigma and decreased quality of life

Challenges

- Management is complex
 - Treat skin manifestations
 - Educate patients/families about disease & stigma
 - Treat & screen for non-skin manifestations (seizures, renal tumors)
 - Making appropriate referrals
- Roadblocks are common
 - Until recently
 - Definitive diagnosis elusive
 - Few effective treatments
 - Little research
 - Few other affected individuals

Advances

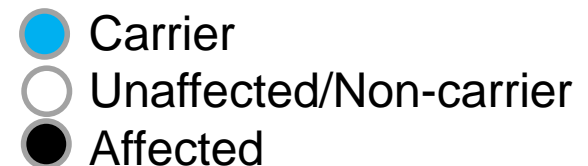
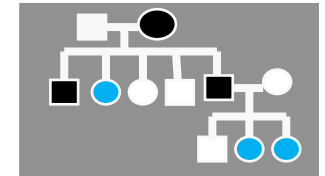
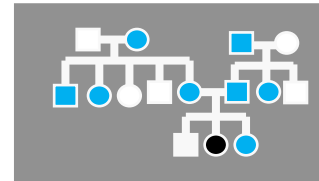
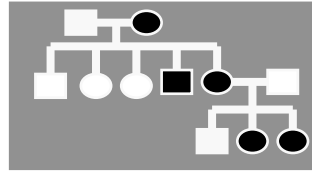
- Diagnosis of rare conditions possible with gene sequencing
- Internet is connecting families and communities
- Online organizations offer virtual support
 - Together Against Genodermatoses (TAG, at www.tag-eu.org)
 - Talk Psoriasis (<http://www.talkpsoriasis.com/>)
 - The National Organization for Albinism and Hypopigmentation (<http://www.albinism.org/awa.html>)
 - Incontinentia Pigmenti International Foundation (<http://www.ipif.org/>)
 - Daily Strength – the eczema support group (<http://www.dailystrength.org/c/Eczema/support-group>)

Genodermatoses Genetics

- 500+ gene mutations cause >560 distinct skin disorders
 - 400 can be traced to a specific gene
 - Significant overlap between disorders → difficult to categorize
- Better understanding of skin physiology/pathophysiology clarifying classification systems.
 - 12 categories based on type of skin lesion
 - Subdivided based on inheritance pattern
- Some “genodermatoses” may be a surprise
 - Osteogenesis Imperfecta
 - Cowden syndrome
 - Hypertriglyceridemia
 - Hemochromatosis

All Inheritance Patterns Represented

- Autosomal dominant
- Autosomal recessive
- X-linked (dominant/recessive)
- Mosaic
- Complex conditions (multiple genes + environment)
- Significant heterogeneity
 - Modifier genes
 - Environmental factors



COMPLEX DISORDERS

Atopic Dermatitis, Psoriasis

Atopic Dermatitis



<http://www.nlm.nih.gov/medlineplus/ency/imagepages/19323.htm>

- More common in industrialized countries (~15% of children)
- Sx's typically manifest in childhood & resolve with age
- Mutations in Filaggrin (*FLG*) gene (4 other suspect genes)
 - Mutation → abnormal enzyme → premature destruction of corneodesmosomes → impaired skin barrier
- Irritants (soap, detergents, dust mites, staph) damage fragile skin → allergens penetrate → inflammatory cascade
- Model for gene/environment interaction & highlights expressivity
 - Not all severely affected patients have *FLG* mutations
 - Not all people with *FLG* mutations develop eczema

Psoriasis



<http://www.nlm.nih.gov/medlineplus/ency/imagepages/2751.htm>

- Autoimmune (T-cell) disorder affecting 2-10% worldwide
 - Environmental trigger + Genetic susceptibility
 - Sx's (itchy, scaly patches) vary widely between individuals
 - Rapid skin maturation → cells pile up → further immune reaction
 - Severe disease: QOL scores similar to other chronic diseases (HTN, depression, CHF, T2DM)
 - Candidate Genes
 - Human Leukocyte Antigen (*HLA*) mutations: *HLA-Cw*0602*
 - Interleukin (*IL*) *IL12B* & *IL23R*
 - Not in HLA family, but involved in immune modulation
 - *IL23R* may play a role in tumorigenesis

MONOGENIC (SINGLE GENE) DISORDERS

Autosomal Dominant: Peutz-Jeghers

Autosomal Recessive: Albinism

X-linked: Incontinentia Pigmenti

Peutz-Jeghers (PJS)



http://openi.nlm.nih.gov/detailedresult.php?img=2769477_1757-1626-0002-0000008865-001&query=peutz-jeghers&fields=all&favor=none&it=ph&sub=none&uniq=0&sp=none&req=4&npos=11&prt=0

- Autosomal Dominant (AD) **cancer syndrome**
- *STK11/LKB1* tumor suppressor gene: Lifetime CA risk 93%
- Skin lesions in childhood (dark blue/brown macules on the fingers, face and perianal area): Begin cancer screening
- Other manifestations
 - Hamartomatous gastrointestinal polyps
 - Small intestine, stomach, large bowel, and nasal passages
 - Rarely cancerous: bleed → anemia, bowel obstruction & intussusception
 - Epithelial cancers
 - Colorectal, gastric, pancreatic, breast, and ovarian cancer

Peutz-Jeghers

- Genetics unclear
 - *STK11/LKB1* mutation inherited
 - De novo
 - Heterogeneous disorder (multiple genes involved)
- Counsel as for other AD disorders
 - Inheritance risk is 50%
 - Prenatal testing available if family mutation known

Albinism



http://openi.nlm.nih.gov/detailedresult.php?img=2211462_1750-1172-2-43-2&query=albinism&fields=all&favor=none&it=ph&sub=none&uniq=0&sp=none&req=4&npos=33&prt=0



http://openi.nlm.nih.gov/detailedresult.php?img=2800870_IJD-54-46-g001&query=albinism&fields=all&favor=none&it=ph&sub=none&uniq=0&sp=none&req=4&npos=3&prt=0

- Autosomal Recessive (AR) disorder; defects in melanin synthesis and/or transport
- Incidence worldwide 1:17,000
 - Sub-Saharan Africa: 1:4000 Zimbabweans; 1:1429 Tanzanians
- Most prevalent form Oculocutaneous albinism (OCA)
 - 4 subtypes (mutations & amount of melanin production)
- Melanin critical for eye development and skin protection. Inadequate melanin
 - Abnormal eye movement, poor visual acuity → difficulty in school
 - High prevalence of skin cancer early in life unless sun screen & protective clothing worn

Albinism

- Social stigma can be profound
 - Very pale skin, pink eyes
 - Struggle in school
 - Stay indoors
 - Wear unusual clothing
- Extreme example
 - Some South African albinos hunted for their body parts (amulets or good luck charms)
 - Affected individuals flee to the “safety” of large, anonymous urban centers
 - Increasing isolation and marginalization

Incontinentia Pigmenti (IP)

- X-linked Dominant disorder (1 affected X = disease)
 - Rare disease (700 women worldwide)
 - Lethal in virtually all males
 - Diagnosis based on clinical features, confirmed by skin biopsy or by gene testing
 - Expression varies widely

Incontinentia Pigmenti (IP)

- Predictable pattern of skin lesions

1. Blistering: birth to ~4 months
2. Wart-like rash: several months
3. Hyperpigmentation: ~6 months on
4. Linear hypopigmentation
 - Slate-gray, blue or brown marbled or wavy lines

- Other features:

- Skin/hair/nails: alopecia, hypodontia, abnormal tooth shape, dystrophic nails
- Eyes: cataracts, retinal detachment and severe vision loss;
- Cognitive delay and intellectual disability
- Skeletal and structural abnormalities: hemivertebrae, scoliosis, spina bifida, syndactyly and acheiria (congenital absence of the hands).



http://openi.nlm.nih.gov/detailedresult.php?img=2946664_jkms-25-1513-g001&query=Incontinentia%20Pigmenti&fields=all&favor=none&it=none&sub=none&uniq=0&sp=none&req=4&npos=11&pri=0



<http://openi.nlm.nih.gov/gridquery.php?q=Incontinentia%20Pigmenti&atab=2&req=0&req=0>

The Role of Nursing

- Nurses play key roles in healthcare
 - Engaged in every life event, present in all healthcare settings, work with all populations
- The public expects nurses to
 - Understand how genetic conditions are inherited
 - Understand the genetics of common conditions (including skin)
 - Help patients navigate the social & ethical issues associated with genetic information
- Individuals expect nurses to
 - Help them navigate physical, emotional, & social consequences
 - School, employment, recreation, intimate relationships
 - Provide rapid access to reputable resources
 - Rapidly locate reputable services and resources
 - Offer suggestions about ways to cope with social stigma

Preparing Nurses

- Key knowledge, education & practice competencies
 - Essentials of Genetic and Genomic Nursing: Competencies, Curricula Guidelines, and Outcome Indicators 2nd Ed (2008)
 - Essential Genetic and Genomic Competencies for Nurses Prepared at the Graduate Level (2012)
- Nurses should be
 - Familiar with genetic disorders commonly seen in their communities and
 - Prepared to develop individualized care plans for patients and families with genetic concerns
 - Prepared to discuss the ethical issues surrounding genetic testing
 - Incidental findings

Conclusion

- Skin disease affects millions world-wide
- Significant morbidity: ↓ QOL, ↑ social stigma & isolation
- Genodermatoses
 - Often poorly understood
 - ELSI issues similar to those with other genetic diseases
- Nurses
 - Link the **science** of genetics and the **human experience** of health and illness
 - Make an enormous positive difference in the lives of patients with hereditary skin disease

QUESTIONS?
COMMENTS?

Friday, April 26, 2013, 3:30-4:30 pm. EST

- ***Genomics and Autism Spectrum Disorder (ASD)*** Dr. Norah Johnson, Marquette University, Wisc., provides an overview of ASD identification, diagnosis, with implications for the family. Genomic contributions to the risk for ASD and highlights of how current research on ASD underscores the complexity of genetic processes involved are presented.
- ***An Update of Childhood Genetic Disorders*** Cynthia Prows Cincinnati Children's Hospital, provides an overview of developments in genetic disorders highlighting the important role for nurses of identification of children with genetic disorders and facilitating access to services. Relevant genomic concepts for nurses who care for infants, children or adolescents with resources to assist in care are provided.
- ***Reserve your Webinar seat for either of these Webinars now at: <https://www1.gotomeeting.com/register/460116969>***